Extended access to cocaine self-administration results in reduced glutamate function within the medial prefrontal cortex.

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Public Summary:
Previous studies have shown that brief access to cocaine yields an increase in D2 receptor binding in the medial prefrontal cortex (mPFC), but that extended access to cocaine results in normalized binding of D2 receptors (i.e. the D2 binding returned to control levels). Extended-access conditions have also been shown to produce increased expression of the NR2 subunit of the N-Methyl-D-aspartate receptor in the mPFC. These results implicate disrupted glutamate and dopamine function within this area. Therefore, in the present study, we monitored glutamate and dopamine content within the mPFC during, or 24 hours after, cocaine self-administration in animals that experienced various amounts of exposure to the drug. Naïve subjects showed decreased glutamate and increased dopamine levels within the mPFC during cocaine self-administration. Exposure to seven 1-hour daily cocaine self-administration sessions did not alter the response to self-administered cocaine, but resulted in decreased basal dopamine levels. While exposure to 17 1-hour sessions also resulted in reduced basal dopamine levels, these animals showed increased dopaminergic, but completely diminished glutamatergic, response to self-administered cocaine. Finally, exposure to 17 cocaine self-administration sessions, the last 10 of which being 6-hour sessions, resulted in diminished glutamatergic response to self-administered cocaine and reduced basal glutamate levels within the mPFC while normalizing (i.e. causing a return to control levels) both the dopaminergic response to self-administered cocaine as well as basal dopamine levels within this area. These data demonstrate directly that the transition to escalated cocaine use involves progressive changes in dopamine and glutamate function within the mPFC.

Scientific Abstract:
Previous studies have shown that brief access to cocaine yields an increase in D2 receptor binding in the medial prefrontal cortex (mPFC), but that extended access to cocaine results in normalized binding of D2 receptors (i.e. the D2 binding returned to control levels). Extended-access conditions have also been shown to produce increased expression of the NR2 subunit of the N-Methyl-D-aspartate receptor in the mPFC. These results implicate disrupted glutamate and dopamine function within this area. Therefore, in the present study, we monitored glutamate and dopamine content within the mPFC during, or 24 hours after, cocaine self-administration in animals that experienced various amounts of exposure to the drug. Naive subjects showed decreased glutamate and increased dopamine levels within the mPFC during cocaine self-administration. Exposure to seven 1-hour daily cocaine self-administration sessions did not alter the response to self-administered cocaine, but resulted in decreased basal dopamine levels. While exposure to 17 1-hour sessions also resulted in reduced basal dopamine levels, these animals showed increased dopaminergic, but completely diminished glutamatergic, response to self-administered cocaine. Finally, exposure to 17 cocaine self-administration sessions, the last 10 of which being 6-hour sessions, resulted in diminished glutamatergic response to self-administered cocaine and reduced basal glutamate levels within the mPFC while normalizing (i.e. causing a return to control levels) both the dopaminergic response to self-administered cocaine as well as basal dopamine levels within this area. These data demonstrate directly that the transition to escalated cocaine use involves progressive changes in dopamine and glutamate function within the mPFC.